Remarks

I. Status of the Claims

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 50-61 are pending in the application, with claim 50 being the independent claim. Claims 60 and 61 are sought to be amended. Support for the amendment to claims 60 and 61 may be found in the specification, for example, at page 17, lines 3-5 and 10-19. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

II. Statement of the Substance of the Interview

Applicants thank Examiner Tekchand Saidha and Supervising Patent Examiner Nashaat Nashed for the courtesy of a personal interview held with Applicants' representatives, Brian J. Del Buono and Shannon A. Carroll, on October 8, 2008, regarding the present application. During that interview, Applicants' representatives discussed the 35 U.S.C. §§ 102(e) and 112, first paragraph, rejections and new matter objections from the Office Action dated July 23, 2008. Examiner Saidha and Supervising Patent Examiner Nashed agreed to consider Applicants' arguments in the present Amendment and Reply Under § 1.111 in view of this discussion.

III. Summary of the Office Action

In the Office Action dated July 23, 2008, the Examiner has made two objections to the specification and two rejections of the claims. Applicants respectfully offer the following remarks concerning each of these elements of the Office Action.

IV. The Rejection Under 35 U.S.C. § 112, First Paragraph Is Traversed

In section 4 of the Office Action at pages 2-3, the Examiner has rejected claims 50-61 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

Under 35 U.S.C. §112, first paragraph, the specification of a patent application must "contain a written description of the invention." "The purpose of this provision is to ensure that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification." *Reiffin v. Microsoft Corp.*, 214 F.3d 1342, 1345 (Fed. Cir. 2000), *reh'g denied*, 214 F.3d 1915, 2000 U.S. App. LEXIS 17769 (Fed. Cir. 2000). However, the courts recognize "that the invention claimed does not have to be described *in ipsis verbis* in order to satisfy the description requirement of § 112." *In re Lukach*, 169 U.S.P.Q. 795, 796 (C.C.P.A. 1971). It is only necessary that the application describe the invention clearly enough that persons of ordinary skill in the art will recognize from the disclosure that Applicants invented compositions including those limitations. *See In re Wertheim*, 541 F.2d 257, 262 (C.C.P.A. 1976).

With respect to numerical range limitations, the analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion

in the original disclosure. *See* MPEP § 2163.05. For example, in *In re Wertheim*, the court held that a disclosure of "25-60% solid content" was adequate written description for a claim to a solid content of "between 35%-60%" although the narrower latter range was not expressly disclosed in the application. *See Wertheim* at 265 (finding that there was no evidence of any distinction in terms of the operability of appellants' process or of the achieving of any desired result between the broad range disclosed in the specification and the narrower claimed range). In addition, in *In re Blaser,* the court held that the appellant's disclosure of heating a reaction to between 60-200 C in their specification was adequate support for the claimed range of 80-200 C that is encompassed within the explicitly disclosed range of 60-200 C. *In re Blaser*, 556 F.2d 534, 538 (CCPA 1977).

Similarly, the present specification discloses that "at least 90% [of the uricase] may be in the tetrameric form; the undesirable aggregates may thus constitute as little as about 10%, 5%, 2%, or less, of the total isolated uricase." *See* specification at page 17, lines 3-5. Thus, the specification clearly discloses compositions in which the proportion of tetrameric uricase present in the composition ranges from at least 90% to 100% (since the total tetrameric uricase can not exceed 100%). Claim 50 is drawn to tetrameric uricase wherein greater than 90% of the uricase is in a tetrameric form, a slightly narrower range encompassed by the disclosed range of at least 90% to 100%.

Furthermore, the specification also discloses that "the purified tetrameric uricase may contain less than about 10% uricase aggregates." *See* specification at page 10, lines 27-29. Thus, if the purified tetrameric uricase contains less than 10% uricase aggregates, by *definition* the uricase preparations *must* contain greater than 90% tetrameric uricase.

Finally as noted above, the specification clearly discloses that "the undesirable aggregates may thus constitute as little as about 10%, 5%, 2%, or less, of the total isolated uricase." *See* specification at page 17, lines 4-5. Thus, if the undesirable aggregates in certain embodiments of the claimed invention may constitute 5% or 2% of the total isolated uricase, it follows that the amount of tetrameric uricase in such embodiments would be at least 95% or at least 98% tetrameric uricase, respectively. Therefore, the specification as filed provides clear support for the currently amended claims.

Hence, the present specification clearly provides sufficient written description to convey to one of ordinary skill that Applicants had possession of the full scope of the claimed invention upon filing of the application. Uricase wherein (1) greater than 90% is in a tetrameric form, (2) at least 95% is in a tetrameric form and (3) at least 98% is in a tetrameric form was in the possession of the Applicants at the time the application was filed and cannot be considered to be new matter. Thus, Applicants respectfully assert that based on the disclosure in the specification and further in view of the holdings of *Wertheim* and *Blaser*, one of ordinary skill in the art would clearly understand that Applicants had invented uricase preparations wherein "greater than 90%" of the uricase is in the tetrameric form.

In view of the foregoing remarks, Applicants respectfully assert that claims 50-61 are fully described in the specification as filed. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, are therefore respectfully requested.

V. The Objections to the Specification Are Traversed

In section 5(a) of the Office Action at page 3, the Examiner has objected to the amendment of the specification to correct a typographical error for allegedly adding new matter to the specification. Applicants respectfully traverse this objection. As indicated in the Second Declaration of Merry R. Sherman Under 37 C.F.R. § 1.132 (hereinafter "the second Sherman declaration") filed September 18, 2007, the present specification describes the commercial preparation of Sigma porcine liver uricase as "Porcine liver uricase . . . obtained from Sigma-Aldrich, St. Louis, MO, catalog No. *U2350* . . . ." (emphasis added). However, as also explained in the second Sherman declaration at page 2, this transposition of numbers is clearly an inadvertent typographical error in the specification, and the catalog number in the specification should correctly read "U3250." As evidence of this typographical error, Applicants submitted copies of a purchase order from Mountain View Pharmaceuticals, Inc. to Sigma-Aldrich (dated May 5, 1998), a packing list from Sigma Aldrich (dated May 5, 1998), an invoice from Sigma Aldrich to Mountain View Pharmaceuticals, Inc. (dated May 5, 1998), and a label from a vial of U3250 (dated "rec'd 5-7-98") as **Exhibits B, C, D and E**, respectively along with the second Sherman Declaration. These exhibits showed that Sigma catalog number U3250 is porcine liver uricase and that Mountain View Pharmaceuticals, Inc., a co-assignee of the present application, ordered and received a vial of Sigma catalog number U3250 in May of 1998. A vial of Sigma catalog number U3250 was used in experiments disclosed in Example 1 of the present application. Therefore, Applicants respectfully assert that the amendment to the specification was made solely to correct a readily apparent and

inadvertent typographical error and does not add new matter to the specification as filed. Thus, Applicants respectfully request that the objection be withdrawn.

In section 5(b) of the Office Action at page 3, the Examiner has objected to the amendment of the specification to add Table 1 for allegedly adding new matter to the specification. Applicants respectfully traverse this objection. As indicated in the Supplemental Amendment filed March 19, 2008, support for the amendment to the substitute specification is found in the originally filed specification, filed April 19, 2001, at page 7, and U.S. Application No. 09/370,084 (hereinafter "the '084 application"), filed August 6, 1999, now U.S. Patent No. 6,576,235, at page 7, to which the present application claims priority under 35 U.S.C. § 120. A "NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION FILED UNDER 37 CFR 1.53(b) -- FILING DATE GRANTED" was mailed for the present application on September 28, 2001. The Notice required "[a] substitute specification in compliance with 37 CFR 1.52" because the papers contained improper margin. When the substitute specification was filed on January 2, 2002, Table 1 was inadvertently omitted from the specification. However, as indicated above, Table 1 was included in the originally filed specification, which was granted a filing date by the USPTO.

In addition, Applicants note that the specification of the '084 application was incorporated by reference in its entirety into the present specification as filed (*see* Preliminary Amendment filed with the present application on April 19, 2001), and the added material was inadvertently omitted from the present application when the substitute specification was filed. Under the USPTO rules of practice, if all or a portion of the specification is inadvertently omitted from an application, but the application

contains a claim under §1.78 for the benefit of a prior-filed non-provisional application that was present on the filing date of the application, and the inadvertently omitted portion of the specification is completely contained in the prior-filed application, the claim under §1.78 shall also be considered an incorporation by reference of the prior-filed application as to the inadvertently omitted portion of the specification. *See* 37 C.F.R. § 1.57(a) and M.P.E.P. § 201.06(c)(IV) at p. 200-26. Therefore, Table 1 was part of the present application filed, as at least via the §120 priority claim to the parent application. Hence, Applicants respectfully assert that the amendment to the specification was made solely to reincorporate Table 1 into the substitute specification, and does not add new matter to the specification as filed. Thus, Applicants respectfully request that the objection be withdrawn.

VI. The Rejection Under 35 U.S.C. § 102(b) Is Traversed

In section 6 and 7 of the Office Action at pages 4-5, the Examiner has maintained the rejection of claims 50-53 and 60-61 under 35 U.S.C. § 102(b) as allegedly being anticipated by Lee *et al.*, *Science 239*: 1288-1291 (1988) (hereinafter "Lee"). Applicants respectfully traverse this rejection.

First, Applicants respectfully point out that as discussed in Applicants' Request to Reopen Prosecution filed September 18, 2007, the Board of Patent Appeals and Interferences (hereinafter "the Board") agreed with Applicants that the Examiner's interpretation of the disclosure of Lee was factually incorrect. *See* Decision on Appeal, filed July 18, 2007 at page 3. As a result, in the Decision on Appeal, the Board designated the rejection of claims 50-53 as a new ground of rejection and effectively

removed the Examiner's reasoning as a basis for rejecting the pending claims. *Id.* at page 6.

However, despite the Board's statements, the Examiner continues to contend that Lee discloses the purification of porcine and murine tetrameric uricases that contain greater than 90% tetrameric uricase because the reference mentions "purification to homogeneity" of porcine and murine urate oxidase. *See* Office Action at page 4 and Lee at page 1289, second column. The Examiner continues to interpret a "homogeneous" preparation of uricase in Lee to mean a preparation that is 100% in the tetrameric form thereby anticipating a preparation in which greater than 90% of the uricase is in tetrameric form. *See* Office Action at page 4. Applicants respectfully disagree with these contentions, and with this interpretation of Lee upon which these contentions are based, for at least the following reasons.

First, contrary to the Examiner's repeated contentions, Lee does not *expressly* disclose preparations of isolated uricase in which greater than 90% of the uricase is in a tetrameric form, as recited by the present claims. Lee only discloses three uricase preparations and *none* of these preparations is expressly disclosed as being greater than 90% in the tetrameric form. First, Lee discloses a commercial preparation of porcine liver uricase from Sigma. Second, Lee also discloses a natural preparation of murine liver uricase. Lee does not indicate *what* form these two uricase preparations were in, let alone that greater than 90% of the uricase preparations were in a tetrameric form. Moreover, as discussed in more detail below, at least the first of these preparations contains significantly less than 90% tetrameric uricase. Third, Lee discloses a uricase preparation where the commercial porcine uricase and natural murine liver uricase have

been "purified to homogeneity" by SDS-PAGE. *See* Lee at pages 1289 and 1291. However, the "homogeneous" uricase preparations of Lee do *not* contain 100% uricase tetramers -- instead they contain isolated monomers, formed from aggregates of isolated uricase by the SDS-PAGE process used in Lee. Thus, as one of ordinary skill would readily appreciate, Lee does not expressly disclose any preparation of isolated uricase in which greater than 90% of the uricase is in a tetrameric form.

Despite the Examiner's repeated assertions to the contrary, Applicants note that the preparations of uricase obtained by Lee for use in the preparative or analytical SDS-PAGE disclosed in that reference are not in the native tetrameric form. This fact is supported by Example 1 in the present specification which discloses that the commercial preparation of porcine liver uricase used in Lee (and also used as a starting material by the inventors of the present application) had to be purified by the methods described in the present application in order to obtain a preparation in which greater than 90% of the uricase was in the tetrameric form. *See* specification at page 20, lines 9-13. The present specification further discloses that natural and recombinant uricases isolated from bacteria, fungi, mammals and plants require purification by the methods described in the present specification in order to obtain an isolated tetrameric uricase preparation in which greater than 90% of the uricase was in the tetrameric form. *See* specification at Examples 4-10. Thus, the commercial preparation of porcine liver uricase and the natural preparation of murine liver uricase disclosed in Lee clearly would not have been expected to contain greater than 90% of the uricase in the tetrameric form.

This conclusion is further supported by the data presented in the Second Declaration Under 37 C.F.R. § 1.132 by Merry R. Sherman, Ph.D., filed September 18,

2007. These data clearly show that the amount of uricase in the tetrameric form that is present in the commercial preparation of porcine liver uricase used both in Lee and as a starting material in Example 1 of the present application was significantly lower than the "greater than 90%" required by the present claims. *See* paragraph 7 and Figure 3 of the second Sherman Declaration. As is shown in Figure 3, and as stated by Dr. Sherman at paragraph 7, the Sigma porcine liver uricase (U3250) contained only about *62% tetramer* prior to purification by the methods described in the present application. Furthermore, these data show that the amount of uricase in the tetrameric form that is present in other isolated commercial, recombinant and natural uricase preparations was significantly lower than the "greater than 90%" required by the present claims -- the Sigma porcine liver uricase (Catalog No. U3377) contained only 86% tetramer; the soybean uricase contained only 65% tetramer; and the *Candida utilis* uricase (Sigma Catalog No. U1878) contained only 55% tetramer, prior to purification by the methods described in the present application. *See* Figures 4 and 5 and paragraphs 8 and 10-11 of the second Sherman Declaration.

Indeed, as Dr. Sherman stated at paragraphs 10 and 16 of the second Sherman declaration and as Figures 1, 2 and 5 clearly show, preparations of uricase that contain greater than 90% of the uricase in the tetrameric form are obtainable only by using isolation methods such as those described in the present application, which are not described in Lee, thereby resulting in the presently claimed uricase preparations. *See* Figures 1, 2, and 5 and paragraphs 10 and 16 of the second Sherman Declaration. Hence, as described in the present specification, and as is clearly shown in the second Sherman Declaration, without specifically purifying the uricase preparations using

methods such as those described in the present specification, the uricase preparations disclosed in Lee would not (and did not) contain greater than 90% tetrameric uricase. Thus, as one of ordinary skill in the art would readily appreciate, Lee does not expressly disclose an isolated tetrameric mammalian uricase having the characteristics recited in the present claims.

In addition, Applicants respectfully assert that Lee does not inherently disclose an isolated tetrameric mammalian uricase, wherein greater than 90% of the uricase is in a tetrameric form as required by the present claims. To rely on an inherency argument, "the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (PTO Bd. Pat. App. Int. 1990) (emphasis in original). This burden has not been met in the present case, since there is no disclosure in Lee, nor any sound scientific reasoning, that uricases containing greater than 90% tetrameric uricase "necessarily flow" from the disclosure in Lee.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). As discussed above, Lee does not expressly or inherently disclose every element of the presently claimed invention. Hence, under *Kalman*, this reference cannot support a rejection under 35 U.S.C. § 102(b). In view of the foregoing remarks, Applicants respectfully assert that Lee does not anticipate claims 50-53. Reconsideration and

withdrawal of the rejection under 35 U.S.C. § 102(b) over Lee therefore are respectfully requested.

VII. Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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